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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 04/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/070,875	SRIVASTAVA ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *1-4,17,24 and 27-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-16,18-23,25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/13/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

HC

DETAILED ACTION

Claims 5 and 24 have been amended.

Claims 1-40 are pending.

1. Applicant's election with traverse of Group II, claims 5-16, 18-23, and 25-28 as they read on a method of treating graft rejection using heat shock proteins that are substantially free of antigenic peptides, and the species elections of gp96, allogeneic relationship of the HSP to the recipient, and the administration of no additional molecules in the reply filed on January 13, 2005 is acknowledged. The traversal is on the ground that US Patent Nos. 5,993,803 and 5,891,653 do not anticipate some of the inventions of the instant application, and as such the finding of Lack of Unity should be withdrawn. This is not found persuasive because US Patents 5,993,803 and 5,891,653 both teach the use of exogenous heat shock proteins to treat graft rejection as indicated in the lack of Unity finding mailed 7/13/2004. Further, Applicant's response does not indicate why Applicant believes that the aforementioned patents do not anticipate some of the inventions claimed in the present invention. It is noted that Applicant's amendment of Claim 24 has necessitated its removal from Group II since it no longer reads on the elected Group. The art search has been extended beyond the elected species of gp96 as the heat shock protein.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-4, 17, 24, and 29-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, and claims 27 and 28 are withdrawn as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on January 13, 2005.

Claims 5-16, 18-23, and 25-26 are under examination in this Office Action.

Applicant is reminded to update the current status of all applications identified in the specification, especially those from which priority is claimed under 35 USC 120 in the first line of the specification. Specifically, the specification should be amended to indicate that USSN 09/393,652 is abandoned.

Information Disclosure Statement

3. Applicant's Information Disclosure Statement received January 13, 2005 has been considered. References A04 and A05 have been considered but have been lined through since they are cited on form 892 mailed July 13, 2004 as part of the Lack of Unity finding.

Claim Objections

4. Claims 7-16, 18-23, and 25-28 are objected to because the indicated claims are dependent upon claims belonging to non-elected groups.

5. Claim 25 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form.

Specifically, claim 5 recites a heat shock protein that is substantially free of antigenic molecules, so the limitation found in claim 25 that said antigenic molecules are not of bacterial origin fails to limit the claim since antigenic molecules are not present.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-16, 18-23, and 25-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

The claimed invention is a method of treating graft rejection using a purified heat shock protein that does not contain complexed antigen. The specification discloses that

both heat shock proteins alone, and heat shock proteins complexed with antigenic molecules are useful in methods of treating graft rejection (see particularly page 1, lines 12-28). Working examples are provided as in experiments 1 and 2, pages 39-42, wherein the administration of the heat shock protein gp96 is seen to have the beneficial effect of inhibiting graft rejection. Both of these experiments use gp96-peptide complexes. No data is provided to indicate that heat shock proteins that do not contain bound antigenic molecules have the same effect in transplantation settings.

Attfield (US Patent 5,891,653, of record on form 892 mailed 7/13/04) teaches that heat shock proteins are to be used in methods of treating graft rejection (see entire document). Attfield further teaches that heat shock proteins which have had their bound peptides removed by the process of purification loose their biological activity to modulate the immune response, and as such are not useful in methods of treating graft rejection (see entire document, particularly column 4, lines 29-47).

Therefore, given the lack of working examples in the specification concerning the treatment of graft rejection using heat shock proteins not complexed to antigenic molecules, and the teachings of the prior art that indicate the necessity of antigenic molecules being bound to heat shock proteins so that they maintain their biological activity of modulating the immune system when used in methods to treat graft rejection as taught by Attfield, a person of skill in the art would not be able to use the claimed invention.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5-16, 18-23, and 25-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Base claim 5 recites the limitation that the purified heat shock protein is "substantially free" of complexed antigenic molecule. The clearest definition in the specification of this limitation appears to be found on page 24, section 5.2.3, wherein it is stated that uncomplexed hsps are substantially free of noncovalently bound antigenic molecules such as peptides. Subsections 5.2.3.1 and 5.2.3.2 then describe methods that can be used to create uncomplexed hsps, but methods for determining the if these method steps were effective in removing the antigenic molecules do not appear to be disclosed. Claim 5 does not recite that the hsps substantially free of antigenic molecules must be obtained by the methods of subsections 5.2.3.1 or 5.2.3.2. Further, the specification teaches that the generation of uncomplexed hsps are not limited to the disclosed methods of low pH treatment or purification in the presence of ATP found in subsections 5.2.3.1 or 5.2.3.2 (see particularly lines 30-34 of page 24 and lines 19-26 of page 25). Since the claims are not limited to a particular method of forming uncomplexed hsps, and since the specification does not clearly indicate how to test for the presence of complexed peptides on hsps to determine if they are "substantially free" of complexed antigenic molecules or indicate what level of contamination with antigenic molecules can be tolerated for the hsp to be judged "substantially free" of antigenic

molecules, a person of skill in the art would not be reasonably apprised of the metes and bounds of the instant claims.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 5-10, 12, 14, 16, 18-22, 25 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Berberian et al., US Patent No. 5,348,945, of record as reference A02 on the IDS filed 1/13/05, see entire document).

Berberian et al. teaches methods enhancing the survival of cells and tissues that are stressed by the administration of the heat shock protein HSP70 (see entire document, particularly claim 1). Situations disclosed by Berberian et al. as being stressful to cells include maintenance of cells, tissues or organs such as heart, lung, liver kidney and skin in culture prior to transplantation, and it is clearly taught that HSP70 is to be administered to such organs to aid in graft survival (see particularly column 3, lines 9-23 and column 4, lines 43-52). Administration of HSP70 can occur before, during or after the cells, tissues or organs are stressed (see particularly column 3, lines 9-68 and column 4, lines 1-52). Berberian et al. teach that due to the highly conserved nature of HSP70, HSP70 from any species of bacteria, animal or plant is useful in the invention, but a preferred embodiment uses mammalian HSP to treat

mammalian cells or tissues (see particularly column 5, lines, lines 5-33). As such, Berberian et al. disclose the use of HSP70 that is and is not an alloantigen of the grafted cell, tissue or organ. The term mammalian as used by Berberian et al. specifically includes humans (see particularly column 3, lines 1-8). Dosages of HSP70 to be administered are provided that coincide with the dosages claimed by Applicant (see particularly column 5, lines 47-54). Berberian et al. disclose the use of purified HSP70 in Example 2 and they do not indicate the presence of any additional molecules (other than the saline solution) complexed with the heat shock protein, or the presence of an additional molecule that modulates the function of an immune system cell in this example (see particularly column 12, lines 15-18).

Therefore, the prior art anticipates the claimed invention.

Double Patenting

10. Claims 5- 7, 9-16, 18-23, and 25-26 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4, 9, 11, 22, 31, and 39 of U.S. Patent No. 6,007,821. Although the conflicting claims are not identical, they are not patentably distinct from each other because they anticipate the claimed invention.

The patented method claims are drawn to a method of treating autoimmune disease using heat shock proteins that are not complexed with antigenic peptides. The specification clearly teaches that immunotherapy using heat shock proteins in

accordance with the invention is useful in treating diabetic patients undergoing islet cell transplantation, such therapy serving to protect the transplanted islet cells from the autoimmune attack that destroyed the original cells (see particularly column 23, lines 12-49 and column 27, lines 20-30). Dosages, timing and routes of administration, and administration of hsps with additional biologically active molecules, are also disclosed (see particularly column 8, lines 18-26, and from line 60 of column 19 to line 40 of column 22).

As such, the use of heat shock proteins not complexed to antigenic molecules for islet cell transplantation anticipates the use of heat shock proteins not complexed to antigenic molecules for use in transplantation settings generically as recited in the instant claims.

11. No claims are allowable.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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March 28, 2005

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